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A DETAIL REVIEW OF EXTEMPORANEOUS COMPOUNDING

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Abstract

It is obvious that large scale manufacturers have very limited opportunity to customize dosage strength and dosage forms for a customer segment that is not substantially big enough due to economies of scale concept of business. Registered and skilled pharmacists in practicing their art of compounding fills in this gap to meet individualized needs. Compounding has always been a basic part of pharmacy practice; the drugs, dosage forms, and equipment or techniques used are the variables. Pharmacists have unique knowledge and skills and are not duplicated by any other profession. Pharmacy activities to individualize patient therapy include compounding and clinical functions. Either function in the absence of the other results in placing pharmacy in a vulnerable position. It is important to entrust a pharmacist's expertise to adjust dosage quantities, frequencies, and even dosage forms to enhance compliance.

Key words

Pharmacy practice, Drugs, Dosage forms, Compounding, Equipment, Formula, Physical and Chemical Compatibility

INTRODUCTION

Pharmacy is a complex mixture of different practices and practice sites. No longer is pharmacy simply community pharmacy or hospital pharmacy. Pharmacy is diverse and offers many opportunities for those willing to look around, find their niche and practice pharmacy to meet the needs of their own community of patients. Most compounding pharmacists appear to be interested and excited about their practices. In fact, many pharmacists intimately involved in pharmaceutical care have now realized the importance of providing individualized patient care through the preparation of patient-specific products. Compounding pharmacy is not for everyone, but as it grows, it will provide an increasingly significant number of pharmacists the excitement and fulfillment of using their innovative and creative skills to solve patient problems.

Evaluation of the Need: Considerations before compounding:

- Commercially availability of drug in dosage form, strength, and packaging
- Ingredients, intended use, dosage, and method of administration concern
- Education, skill and expertise to drug compounding

Mohiuddin et.al / UJPSR / 4 (1), 2018, 48-62
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- Proper equipment, supplies, chemicals and the guidelines delineated in us pharmacopeia
- An alternative by which the patient will receive a benefit
- Safety of the compounded product
- Patient necessary storage facility, if required,
- Necessary calculations to prepare the product
- Necessary documentation to complete preparation
- Literature reference that might provide information on use, preparation, stability, administration
- Expected duration of therapy
- Some basic quality control to check the product prior to dispensing (eg, capsule weight variation, pH, visual observations)
- Ingredient identity, quality, and purity
- Corrective methods
- Physico-chemical incompatibilities **[1]**

Economic Considerations: There are at least two different economic considerations in making the decision to compound prescriptions; these include
(1) pharmacist compensation and
(2) health-care costs.

The pricing of a compounded prescription should include consideration for pharmacodynamic and pharmaco therapeutic decision making, formulation expertise, time, and reimbursement of materials. Compounding prescriptions can be attractive professionally and financially **[2].** Compounding prescriptions can be a way of lowering the cost of drug therapy. In some cases, it is less expensive for the pharmacist to prepare a specific prescription for the patient, which may mean the difference between the patient actually obtaining the drug or doing without it. If compounding a prescription results in a patient being able to afford the drug therapy, it must be considered **[3].**

Compounding Factors

Stability: One key factor in compounding prescriptions is stability. The more common types of stability of which compounding pharmacists should be aware include chemical, physical, and microbiological. Whereas commercially manufactured products are required to possess an expiration date, compounded products are assigned a beyond-use date. There are numerous sources of information that can be used for determining an appropriate beyond-use date, such as chemical companies, manufacturers literature, laboratory data, journals, and published books on the subject. Generally, most pharmacists prepare or dispense small quantities of compounded products; recommend storage at room, cool, or cold temperatures; and use a conservative beyond-use date. For non aqueous liquids and solid formulations (for which the manufactured drug product is the source of active ingredient): The beyond-use date is not later than 25% of the time remaining until the product's expiration date or 6 months, whichever is earlier.A USP or NF substance is the source of active ingredient. The beyond-use date is not later than 6 months.For water-containing formulations (prepared from

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ingredients in solid form): The beyond-use date is not later than 14 days when stored at cold temperatures. For all other formulations. The beyond-use date is not later than the intended duration of therapy or 30 days, whichever is earlier. These beyond-use date limits may be exceeded when there is supporting valid scientific stability information that is directly applicable to the specific preparation (ie, the same drug concentration range, pH, excipients, vehicle, water content) **[4, 5].**

Quality Control: One of the fastest growing and most important areas of pharmaceutical compounding is that of quality control. Quality must be built-in to the preparation from the beginning steps to evaluating the final preparation. There are several quality control tests that can be done within the pharmacy and others can be sent to a contract laboratory. The following quality control tests can be considered for the respective dosage forms.

Oral and topical liquids (solutions, suspensions, emulsions): Weight/volume, pH, specific gravity, active drug assay, globule size range, rheological properties/pour ability, physical observation(color, clarity), physical stability (discoloration, foreign materials, gas formation, mold growth).

Hard Gelatin Capsules: Weight-overall average weight, weight individual weight variation, dissolution of capsule shell, disintegration and/or dissolution of capsule contents, active-drug assay, physical appearance (color, uniformity, extent of fill, locked),physical stability (discoloration, changes in appearance).

Ointments, Creams and Gels: Theoretical weight compared to actual weight, pH, specific gravity, active drug assay, physical observations (color, clarity, texture-surface, texture-spatula spread, appearance, feel) and rheological properties.

Suppositories, Troches, Lollipops and Sticks: Weight, specific gravity, active drug assay, physical observation (color, clarity, texture of surface, appearance, feel), melting test, dissolution test, physical stability.

Parenteral preparations: Weight/volume, physical observation, pH, specific gravity, osmolality, assay, color, clarity, particulate matter, sterility, pyrogenicity **[6, 7].**

Compounding Support: Numerous agencies, companies, organizations, etc, are available to assist pharmacists in compounding. Information, chemicals, supplies, and equipment are readily available. Chemical and supply companies have increased in size and number in recent years and many provide information on compounding, incompatibilities, and stability. Specialty compounding organizations have developed over recent years and generally provide full-line services and products to the compounding pharmacist. Many national organizations provide continuing professional education programs in both non-sterile and sterile compounding. These entities provide services to compounding pharmacists ranging from selling only compounding aids to providing only chemicals. Others offer additional services to include formulas as well as consulting expertise by telephone or via the internet. This service can assist

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in the process of compounding a particular product that may be difficult.

Training And Experience: Pharmacists involved in upgrading and increasing the traditional aspects of extemporaneous compounding need to keep current with all the new tools of their trade, retrieve the old from storage, and put in a bit of practice using their scientific background and their art before they will be comfortable in exhibiting their skills. When considering providing additional services of compounding in an institution, pharmacists should not expect that this will change a great deal of their practice in time consumed for compounding.

Equipment: The equipment needed will be determined by the type and extent of the services one chooses to provide. Many pharmacies already have clean air environments (eg, laminar air flow hoods, isolation barrier systems) where aseptic compounding of sterile solutions is performed. These same units can be used to compound other sterile preparations such as eye drops. A balance, preferably electronic, is essential. Ointments labs (ie, pill tiles), along with spatulas of different types and materials, should be purchased. A few mortars and pestles (ie, glass, ceramic, plastic) and some glassware should be secured. It may not be necessary to buy a roomful of equipment, but one should purchase what is needed to start the service and should build on it as the service grows and expands to different arenas. Much of the equipment used today in compounding has changed. Today, electronic balances are used more often than torsion balances; micro-pipets are commonplace; and ultra-freezers are sometimes required in addition to standard refrigerator freezers. This area is constantly changing and the compounding pharmacist should be aware of the available technology to prepare accurate and effective prescriptions. Becoming acquainted with the local representative for a laboratory supply company is helpful.

Environment: A separate area for traditional compounding is recommended, rather than simply cleaning off as mall area of the dispensing counter. The compounding pharmacist needs a clean, neat, well-lit and quiet working area. If aseptic compounding is considered, a clean air environment (e.g., laminar air flow hood, isolation barrier system) should be used. The actual facility to be used depends on the level and volume of compounding to be done.

Formulas: Consistency of the compounded product is important. Formulas should be developed or obtained and tried to assure that each time an extemporaneous product is prepared, the methods used, ingredients added, and the order of steps is documented. This accomplishes three things. First, it provides the methodology for each person involved or requested to provide such service the information necessary to do so properly. Second, it provides consistency from batch to batch. Third, if the product does not turn out the way expected, a stepwise methodology exists for reviewing and determining what happened and if revisions and improvements are needed.

Chemicals and Supplies: If one is going to prepare a topical product, a vehicle (eg, cream,

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ointment, gel) and the active ingredients (eg, either finely ground product from an available tablet or injection or pharmaceutical-grade chemicals) would be required. One needs proper dispensing containers for the medication. In short, a relationship with providers that carry chemicals and supplies is important. Pharmacists have been using chemicals and other materials for prescription compounding throughout history. In the past, these chemicals and materials have been obtained from natural products, raw materials, and household ingredients. Today, compounding pharmacists use chemicals from various reliable commercial sources, depending on their availability **[8].**

Types of Compounding

Ambulatory-Care Compounding: If individuals can walk, they are considered mobile or ambulatory (i.e., they are not bedridden). Consequently, most pharmacists are involved in ambulatory care, and most ambulatory patients are outpatients. Actually, the term can also be applied to home-care patients and even institutionalized patients who are mobile. One general characteristic of ambulatory patients is that they are generally responsible for obtaining their own medication, storing it, preparing it (if necessary), and taking it. It seems almost incongruous that in health care today as we become more aware that patients are individuals, respond as individuals, and must be treated as individuals that some health-care providers appear to be grouping patients into categories. They are grouped in categories for treatment, for reimbursement from a third party, or for determining levels of care in managed-care organizations and using fixed-dose products provided by pharmaceutical manufacturers that are available because the marketing demand is sufficiently high to justify their manufacture and production. Why should the availability or the lack of availability of a specific economically profitable commercially available product dictate the therapy of a patient? Pharmacists have an opportunity to extend their activities in patient care as the emphasis continues to shift from inpatient care to ambulatory care. Ambulatory care, however, is so diverse and involves so many disciplines that sometimes it is difficult to understand it; and, it changes rapidly. Also, ambulatory care could generally encourage a team approach to health improvement, prevention, health maintenance, risk assessment, early detection, management, curative therapy, and rehabilitation. Ambulatory care offers various opportunities for individualizing patient care through pharmaceutical compounding. In fact, it is the area where most compounding pharmacists' practice. Pharmacists' roles in ambulatory care patients can include, among others:

- Dispensing
- Compounding
- Counseling
- Minimizing medication errors
- Compliance enhancement
- Therapeutic drug monitoring
- Minimizing expenditures

Most reimbursement for ambulatory patients comes from the dispensing or the compounding process.

Mohiuddin et.al / UJPSR / 4 (1), 2018, 48-62
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Little financial consideration is given to counseling, minimizing medication errors, compliance enhancement and therapeutic monitoring. However, these activities are important and should be performed. Because of the unique nature of compounded medications, counseling is an absolute must for these patients. From the above discussion of the activities of ambulatory care pharmacists, it should be evident that extemporaneous compounding can be vitally important in ambulatory patient care **[8, 9].**

Hospital Pharmacy Compounding: The ever-present responsibility of the health-care industry is to provide the best available care for the patient, using the best means to do so, and providing that care in a conducive environment. This must be sufficiently economical to not put the institution in jeopardy of being unable to continue to provide the services to the community they serve. This requires cooperation on the part of the hospital administration, the medical staff, and the employees (nurses and pharmacists in particular as regards to medication usage) and must involve the patient. One of the effective means by which hospitals, and therefore hospital pharmacies, can meet these challenges is to consider expanding extemporaneous compounding services within the hospital pharmacy. Pharmaceutical care and pharmaceutical compounding can provide cost savings to the hospital while providing needed options to the physician through problem-solving approaches and stimulating the hospital pharmacist through new challenges that allow the expression of both their skills and their art **[8,10].**

Veterinary Compounding: The first symposium on veterinary compounding was a significant forum for discussion by experts and was a pivotal point in the history of veterinary compounding, occurring in September 1993.16 the meeting was important because it assembled an impressive group of experts on veterinary compounding, who then set about explaining and defining the roles of the veterinarian and the pharmacist **[11].**

Nuclear Pharmacy Compounding: Nuclear pharmacy is a specialty practice of pharmacy that has been defined as a patient-oriented service that embodies the scientific knowledge and professional judgment required for improving and promoting health through assurance of the safe and efficacious use of radioactive drugs for diagnosis and therapy. Radioactive drugs, commonly referred to as radiopharmaceuticals, are a special class of drugs that are regulated by the FDA. They are unique in that they contain an unstable nuclide (radioactive nuclide) as a part of the compound designed to localize in an organ or tissue. Since radiopharmaceuticals are radioactive, the Nuclear Regulatory Commission or a similarstate agency is involved in regulatory matters relevant to radiopharmaceuticals **[12-14].**

Regulations and Guidelines Good Compounding Practices Applicable to State-Licensed Pharmacies: The following Good Compounding Practices (GCPs) are meant to apply only to the compounding of drugs by state-licensed pharmacies.

Subpart A-General Provisions: The recommendations contained herein are considered

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the minimum current good compounding practices for the preparation of drug products by state-licensed pharmacies for dispensing or administration to humans or animals. The following definitions from the NABP (National Association of Boards of Pharmacy) Model State Model State Pharmacy Act apply to these GCPs. States may wish to insert their own definitions to comply with State Pharmacy Practice Acts.

Compounding: The preparation, mixing, assembling, packaging, or Labeling of a Drug or Device (I) as the result of a Practitioner's Prescription Drug Order or initiative based on the Practitioner/patient/Pharmacist relationship in the course of professional practice, or(ii) for the purpose of, or as an incident to, research, teaching or chemical analysis and not for sale or Dispensing. Compounding also includes the preparation of Drugs or Devices in anticipation of Prescription Drug Orders based on routine, regularly observed prescribing patterns.

Manufacturing: The production, preparation, propagation, conversion or processing of a Drug or Device, either directly or indirectly, by extraction from substances of natural origin or independently by means of chemical or biological synthesis, and includes any packaging or repackaging of the substance(s) or Labeling or relabeling of its container, and the promotion and marketing of such Drugs or Devices. Manufacturing also includes the preparation and promotion of commercially available products from bulk compounds for resale by pharmacies, Practitioners, or other Persons **[15, 16].**

Component: Any ingredient intended for use in the compounding of a drug product, including those that may not appear in such product. Based on the existence of a Pharmacist/patient/Prescriber relationship and the presentation of a valid Prescription, Pharmacists may Compound, in reasonable quantities, Drug products that are commercially available in the marketplace. Pharmacists shall receive, store, or use drug substances for compounding that have been made in an FDA-approved facility. Pharmacists shall also receive, store, or use drug components in compounding prescriptions that meet official compendia requirements. If neither of these requirements can be met, pharmacists shall use their professional judgment to procure alternatives. Pharmacists may compound drugs in very limited quantities prior to receiving a valid prescription based on a history of receiving valid prescriptions that have been generated solely within an established pharmacist/patient/prescriber relationship, and provided that they maintain the prescriptions on file for all such products compounded at the pharmacy(as required by State law). The compounding of inordinate amounts of drugs in anticipation of receiving prescriptions without any historical basis is considered manufacturing. Pharmacists shall not offer compounded drug products to other State-licensed persons or commercial entities for subsequent resale, except in the course of professional practice for a prescriber to administer to an individual patient. Compounding pharmacies/pharmacists may advertiser otherwise promote the fact that they

Mohiuddin et.al / UJPSR / 4 (1), 2018, 48-62
e ISSN: 2454-3764
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provide prescription compounding services; however, they shall not solicit business (e.g., promote, advertise, or use salespersons) to compound specific drug products. The distribution of inordinate amounts of compounded products pursuant to a legitimate prescription out of state without a prescriber/patient/pharmacist relationship is considered manufacturing. Pharmacists engaged in the compounding of drugs shall operate in conformance with applicable State law regulating the practice of pharmacy **[17, 18].**

Subpart B-Organization and Personnel: As in the dispensing of all prescriptions, the pharmacist has the responsibility and authority to inspect and approve or reject all components, drug product containers, closures, in-process materials, labeling and the authority to prepare and review all compounding records to assure that no errors have occurred in the compounding process. The pharmacist is also responsible for the proper maintenance, cleanliness and use of all equipment used in prescription compounding practice. All pharmacists who engage in compounding of drugs, shall be proficient in the art of compounding and shall maintain that proficiency through current awareness and training. Also, every pharmacist who engages in drug compounding must be aware of and familiar with all details of the Good Compounding Practices. Personnel engaged in the compounding of drugs shall wear clean clothing appropriate to the operation being performed. Protective apparel, such as a coat/jacket, apron or hand or arm coverings, shall be worn as necessary to protect drug products from contamination. Only personnel authorized by the responsible pharmacist shall be in the immediate vicinity of the drug compounding operation. Any person shown at any time (either by medical examination or pharmacist determination)to have an apparent illness or open lesion(s) that may adversely affect the safety or quality of a drug product being compounded shall be excluded from direct contact with components, drug product containers, closures, in-process materials and drug products until the condition is corrected or determined by competent medical personnel not to jeopardize the safety or quality of the products(s) being compounded. All personnel who normally assist the pharmacist in compounding procedures shall be instructed to report to the pharmacist any health conditions that may have an adverse effect on drug products **[19-21].**

Subpart C: Drug Compounding Facilities: Pharmacies engaging in compounding shall have a specifically designated and adequate area (space) for the orderly placement of equipment and materials to be used to compound medications. The drug compounding area for sterile products shall be separate and distinct from the area used for the compounding or dispensing of non-sterile drug products. The area(s) used for the compounding of drugs shall be maintained in a good state of repair. Bulk drugs and other materials used in the compounding of drugs must be stored in adequately labeled containers in a clean, dry area or, if required, under proper refrigeration. Adequate lighting and ventilation shall be provided in all drug compounding areas. Potable water shall be

Mohiuddin et.al / UJPSR / 4 (1), 2018, 48-62
e ISSN: 2454-3764
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supplied under continuous positive pressure in a plumbing system free of defects that could contribute contamination to any compounded drug product. Adequate washing facilities, easily accessible to the compounding area(s) of the pharmacy, shall be provided. These facilities shall include, but not be limited to, hot and cold water, soap or detergent, and air-driers or single-use towels. The area(s) used for the compounding of drugs shall be maintained in a clean and sanitary condition. It shall be free of infestation by insects, rodents and other vermin. Trash shall be held and disposed of in a timely and sanitary manner. Sewage, trash and other refuse in and from the pharmacy and immediate drug compounding area(s) shall be disposed of in a safe and sanitary manner.

***Sterile Products/Radiopharmaceuticals*:** If sterile (aseptic) products are being compounded, conditions set forth in the NABP Model Rules for Sterile Pharmaceuticals must be followed. If radiopharmaceuticals are being compounded, conditions set for thin the NABP Model Rules for Nuclear/Radiologic Pharmacy must be followed.

Special Precaution Products: If drug products with special precautions for contamination, such as penicillin, are involved in a compounding operation, appropriate measures, including either the dedication of equipment for such operations or the meticulous cleaning of contaminated equipment prior to its return to inventory, must be used in order to prevent cross-contamination.

Subpart D-Equipment: Equipment used in the compounding of drug products shall be of appropriate design, adequate size, and suitably located to facilitate operations for its intended use and for its cleaning and maintenance. Equipment used in the compounding of drug products shall be of suitable composition so that surfaces that contact components, in-process materials, or drug products shall not be reactive, additive or absorptive so as to alter the safety, identity, strength, quality or purity of the drug product beyond that desired. Equipment and utensils used for compounding shall be cleaned and sanitized immediately prior to use to prevent contamination that would alter the safety, identity, strength, quality or purity of the drug product beyond that desired. In the case of equipment, utensils and containers/closures used in the compounding of sterile drug products, cleaning, sterilization and maintenance procedures as set forth in the NAB Model Rules for Sterile Pharmaceuticals must be followed. Previously cleaned equipment and utensils used for compounding drugs must be protected from contamination prior to use. Immediately prior to the initiation of compounding operations, they must be inspected by the pharmacist and determined to be suitable for use. Automatic, mechanical or electronic equipment or other types of equipment or related systems that will perform a function satisfactorily may be used in the compounding of drug products. If such equipment is used, it shall be routinely inspected, calibrated (if necessary) or checked to assure proper performance **[8, 22].**

Subpart E: Control of Components and Drug Product Containers and Closures: Components, drug product containers and closures, used in the

Mohiuddin et.al / UJPSR / 4 (1), 2018, 48-62
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compounding of drugs shall be handled and stored in a manner to prevent contamination. Bagged or boxed components of drug product containers and closures used in the compounding of drugs shall be stored off the floor in such a manner as to permit cleaning and inspection. Drug product containers and closures shall not be reactive, additive or absorptive so as to alter the safety, identity, strength, quality or purity of the compounded drug beyond the desired result. Components, drug product containers and closures for use in the compounding of drug products shall be rotated so that the oldest stock is used first. Container closure systems shall provide adequate protection against foreseeable external factors in storage and use that can cause deterioration or contamination of the compounded drug product. Drug product containers and closures shall be clean and, where indicated by the intended use of the drug, sterilized and processed to remove pyrogenic properties to assure that they are suitable for their intended use. Drug product containers and closures intended for the compounding of sterile products must be handled, sterilized, stored, etc in keeping with the NABP Model Rules for Sterile Pharmaceuticals. Methods of cleaning, sterilizing and processing to remove pyrogenic properties shall be written and followed for drug product containers and closures used in the preparation of sterile pharmaceuticals, if these processes are performed by the pharmacist, or under the pharmacist's supervision following the NABP Model Rules for Sterile Pharmaceuticals **[8, 23, 24].**

Subpart F-Drug Compounding Controls: There shall be written procedures for the compounding of drug products to assure that the finished products have the identity, strength, quality and purity they purport or are represented to possess. Such procedures shall include a listing of the components (ingredients), their amounts (in weight or volume), the order of component addition and a description of the compounding process. All equipment and utensils and the container/closure system, relevant to the sterility and stability of the intended use of the drug, shall be listed. These written procedures shall be followed in the execution of the drug compounding procedure. Components for drug product compounding shall be accurately weighed, measured or subdivided as appropriate. These operations should be checked and rechecked by the compounding pharmacist at each stage of the process to ensure that each weight or measure is correct as stated in the written compounding procedures. If a component is removed from the original container to another (eg, a powder is taken from the original container, weighed, placed in a container and stored in another container) the new container shall be identified with the:

(a) component name, and

(b) weight or measure.

To assure the reasonable uniformity and integrity of compounded drug products, written procedures shall be established and followed that describe the tests or examinations to be conducted on the product being compounded (e.g., compounding of capsules). Such control procedures shall be

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established to monitor the output and to validate the performance of those compounding processes that may be responsible for causing variability in the final drug product. Such control procedures shall include, but are not limited to, the following (where appropriate):

(a) capsule weight variation;

(b) adequacy of mixing to assure uniformity and homogeneity;

(c) clarity, completeness or pH of solutions.

Appropriate written procedures designed to prevent microbiological contamination of compounded drug products purporting to be sterile shall be established and followed. Such procedures shall include validation of any sterilization process **[19, 25].**

Subpart G-Labeling Control of Excess Products: In the case where a quantity of a compounded drug product in excess of that to be initially dispensed in accordance with Subpart A is prepared, the excess product shall be labeled or documentation referenced with the complete list of ingredients (components), the preparation date, and the assigned expiration date based upon professional judgment, appropriate testing, or published data. It shall also be stored and accounted for under conditions dictated by its composition and stability characteristics (eg, in a clean, dry place on a shelf or in the refrigerator) to ensure its strength, quality and purity. At the completion of the drug finishing operation, the product shall be examined for correct labeling.

Subpart H-Records and Reports: Any procedures or other records required to be maintained in compliance with these Good Compounding Practices shall be retained for the same period of time as each State requires for the retention of prescription files. All records required to be retained under these Good Compounding Practices, or copies of such records, shall be readily available for authorized inspection during the retention period at the establishment where the activities described in such records occurred. These records or copies thereof shall be subject to photocopying or other means of reproduction as part of such inspection.

Identifying Errors and Cause

Variation in performance can produce unexpected and adverse outcomes. Sentinel events, as defined by the Joint Commission on Accreditation of Health Care Organizations (JCAHO), are unexpected occurrences involving death or serious physical or psychological injury or the risk thereof. Error investigation requires a rigorous, systematic approach to evaluate basic or causal factors for variation in system performance. Root cause analysis, a technique utilized to identify the fundamental reason for system failure, focuses on systems and processes rather than on individuals involved in the system. The time required might vary depending on how busy the pharmacy is, whether the prescription is a refill or new order, if the patient is new to the clinic, if the product requires compounding, or even the time of day the prescription is presented to the pharmacy staff. Variation in the process of providing a prescription is inherent, resulting from common causes such as staffing levels, availability of patient information,

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or access to medication supply. A process that varies only because of common causes is said to be stable. The level of performance of a stable process, or the range of the common cause variation, can only be changed by redesigning the process. A special cause is variation which occurs from unusual circumstances or events that are difficult to predict. Special cause is not inherent as part of the system; it is usually as a result of external influence and not part of the system as designed. The results of special cause variation often lead to process instability which is best described as intermittent and unpredictable. Examples of special cause variation in the medication use process might include manufacturer recalls, compounding equipment or automation failure, widespread professional staff sick calls, environmental/natural disaster or other acts of God that lead to failure. These special causes should be identified and eliminated. However, this will only affect the abnormal performance in that process. It cannot prevent the special cause from recurring **[26-29].**

CONCLUSION

Pharmacy compounding provides pharmacists with a unique opportunity to practice their time-honored profession. It is becoming an even more important part of pharmacy practice in the future, including those involved in community and hospital care, nursing care, home care, veterinary and other specialty practices. It is a practice where the clinical expertise can be merged with the scientific expertise of pharmacists to make a visible pharmaceutical care. Pharmacists are to be encouraged more in compounding but should be aware of the core of formulating a specific drug product for a specific patient. This is important in providing pharmaceutical care.

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Compliance with the Ethical Issues

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•Competing interests

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